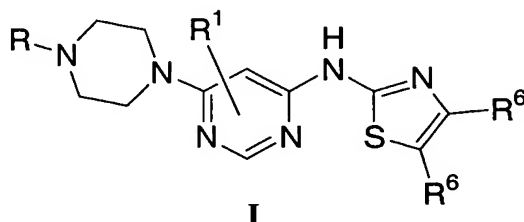


WHAT IS CLAIMED IS:

1. A process for preparing substituted thiazolyl-amino pyrimidinyl piperazines of Formula I:



wherein

R is H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>0</sub>-C<sub>6</sub>)alkyl-NR<sup>a</sup>R<sup>b</sup>, or (C<sub>0</sub>-C<sub>6</sub>)alkyl-C(O)N(R<sup>e</sup>)<sub>2</sub>;

R<sup>1</sup> is H, or unsubstituted or substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl;

R<sup>6</sup> is independently selected from H, phenyl, halogen, CN, and pyridyl, said phenyl and pyridyl optionally substituted with one to three substituents selected from R<sup>7</sup>;

R<sup>7</sup> is independently selected from:

- 1) O<sub>r</sub>(C=O)<sub>s</sub>NR<sup>a</sup>R<sup>b</sup>,
- 2) (C=O)<sub>r</sub>O<sub>s</sub>aryl,
- 3) (C=O)<sub>r</sub>O<sub>s</sub>-heterocyclyl,
- 4) halogen,
- 5) OH,
- 6) O(C<sub>1</sub>-C<sub>3</sub>)perfluoroalkyl,
- 7) (C<sub>1</sub>-C<sub>3</sub>)perfluoroalkyl,
- 8) (C=O)<sub>r</sub>O<sub>s</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl,
- 9) CO<sub>2</sub>H,
- 10) CN,
- 11) (C<sub>1</sub>-C<sub>6</sub>)alkyl-NR<sup>a</sup>R<sup>b</sup>, and
- 12) (C<sub>1</sub>-C<sub>6</sub>)alkyl-heterocyclyl,

wherein r and s are independently 0 or 1, and said aryl, heterocyclyl and alkyl are optionally substituted with one to three substituents selected from R<sup>d</sup>;

$R^a$  and  $R^b$  are independently:

- 1) H,
- 2)  $(C=O)_r(C_1-C_{10})$ alkyl,
- 3)  $S(O)_2R^c$ ,
- 5 4)  $(C=O)_r$ heterocyclyl,
- 5)  $(C=O)_r$ aryl, and
- 6)  $CO_2R^c$ ,

wherein  $r$  is 0 or 1 and said alkyl, heterocyclyl, and aryl optionally substituted with one or more substituents selected from  $R^d$ ;

10

$R^c$  is independently selected from  $(C_1-C_6)$ alkyl, aryl, and heterocyclyl;

$R^d$  is independently selected from:

- 1)  $(C=O)_rO_s(C_1-C_{10})$ alkyl, wherein  $r$  and  $s$  are independently 0 or 1,  
 15 optionally substituted with up to three substituents selected from OH,  
 $(C_1-C_6)$ alkoxy, halogen, heterocyclyl, CN, oxo,  $N(R^e)_2$  and  $S(O)_2R^c$ ,
- 2)  $O_r(C_1-C_3)$ perfluoroalkyl,
- 3)  $(C_0-C_6)$ alkylene- $S(O)_mR^c$ , wherein  $m$  is 0, 1, or 2,
- 4) OH,
- 20 5) halo,
- 6) CN,
- 7)  $(C_0-C_6)$ alkylene-aryl, optionally substituted with up to three  
 substituents selected from  $R^e$ ,
- 8)  $(C_0-C_6)$ alkylene-heterocyclyl, optionally substituted with up to three  
 25 substituents selected from  $R^e$ ,
- 9)  $C(O)R^c$ ,
- 10)  $CO_2R^c$ ,
- 11)  $C(O)H$ ,
- 12)  $N(R^e)_2$ , and
- 30 13)  $CO_2H$ ;

$R^e$  is independently selected from:

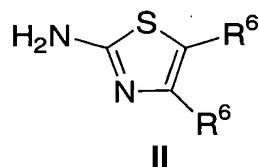
- 1) H,

- 2) (C<sub>1</sub>-C<sub>6</sub>)alkyl, optionally substituted with one or more substituents selected from OH, heterocyclyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halogen, CN, oxo, N(R<sup>f</sup>)<sub>2</sub> and S(O)<sub>2</sub>R<sup>c</sup>,
- 3) aryl, optionally substituted with one or more substituents selected from OH, heterocyclyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halogen, CN, N(R<sup>f</sup>)<sub>2</sub> and S(O)<sub>2</sub>R<sup>c</sup>,
- 4) heterocyclyl, optionally substituted with one or more substituents selected from OH, heterocyclyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halogen, CN, oxo, N(R<sup>f</sup>)<sub>2</sub> and S(O)<sub>2</sub>R<sup>c</sup>, and
- 5) S(O)<sub>2</sub>R<sup>c</sup>;
- 10 said heterocycle optionally substituted with one or more substituents selected from OH, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halogen, CN, oxo, N(R<sup>f</sup>)<sub>2</sub> and S(O)<sub>2</sub>R<sup>c</sup>; and

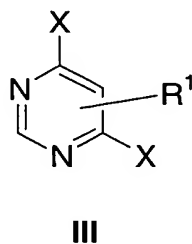
R<sup>f</sup> is independently selected from H, aryl and (C<sub>1</sub>-C<sub>6</sub>)alkyl;

- 15 which comprises the steps of:

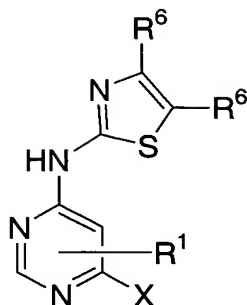
- a) reacting a compound of Formula II



with a compound of Formula III

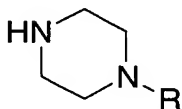


- 20 (wherein X is halo), to provide a compound of Formula IV

**IV**

;

b) reacting the compound of Formula IV with a compound of  
Formula V

**V**

; and

- 5 c) isolating the compound of Formula I.
2. The process according to Claim 1 which comprises the steps  
of:
- 10 a) adding the compounds of Formula II and Formula III and a  
phosphate to a first solvent;
- b) isolating the compound of Formula IV;
- c) adding the compound of Formula IV and a trialkylamine to a  
mixture of the compound of Formula V in a second solvent;  
and
- 15 d) isolating the compound of Formula I.

3. The process according to Claim 2 wherein the first solvent is  
selected from unchlorinated or chlorinated hydrocarbons, nitriles, ethers, polar aprotic  
solvents or mixtures thereof.

20

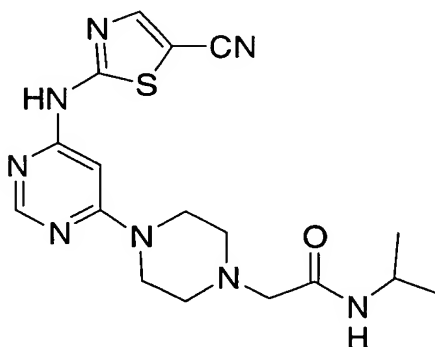
4. The process according to Claim 2 wherein the second solvent is selected from water, alcohols, unchlorinated or chlorinated hydrocarbons, nitriles, ketones, ethers, polar aprotic solvents or mixtures thereof.

5. The process according to Claim 2 wherein the unsubstituted or substituted amine is selected from unsubstituted or substituted arylamine, unsubstituted or substituted heteroarylamine, unsubstituted or substituted C<sub>1</sub>-C<sub>6</sub> alkylamines, ammonia, H<sub>2</sub>N-R<sup>a</sup>C(O)OR and H<sub>2</sub>N-R<sup>a</sup>SR.

6. The process according to Claim 1 which comprises the steps of:

- a) adding the compounds of Formula II and Formula III and a carbonate to a first solvent;
- b) isolating the compound of Formula IV;
- c) adding the compound of Formula IV and a trialkylamine to a mixture of the compound of Formula V in a second solvent; and
- d) isolating the compound of Formula I.

7. A process for preparing 2-(4-{6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl}piperazin-1-yl)-N-isopropylacetamide



which comprises the steps of:

5

- a) adding 2-amino-5-cyanothiazole, dichloropyrimidine, and  $K_3PO_4$  to DMF to provide 2-[(6-chloropyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile;
- b) adding 2-[(6-chloropyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile and triethylamine to N-Isopropyl-2-piperazin-1-ylacetamide in n-butanol; and
- c) isolating 2-(4-{6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl}piperazin-1-yl)-*N*-isopropylacetamide.

10